

Reproductive Effects of Male Dioxin Exposure

The Use of Offspring Sex Ratios to Detect Reproductive Effects of Male Exposure to Dioxins

Toppari et al. [EHP 104(suppl 4): 741–803(1996)], writing of the possible effects of dioxin, remark that no reproductive disorders in adults have been described after the accident in 1976 in Seveso, Italy. Publications since the submission of this paper put this assertion into perspective.

There is good evidence that the sex ratio (proportion male at birth) of mammalian (including human) offspring is partially controlled by the hormone levels of both parents around the time of conception (1). Egeland et al. (2) reported that men exposed to dioxin had low testosterone and high gonadotropin levels. Noting that this hormone profile is associated with female offspring, I predicted that exposure to dioxin would be associated with the subsequent births of excess daughters (3). This has since been confirmed with respect to the accident at Seveso (4) and to the workers exposed to wood preservatives contaminated by dioxin (5). The former study reported that a few heavily exposed parents produced a substantial and highly significant excess of daughters. The latter paper reported a slight but significant excess of daughters born to a large sample of men of whom it may be presumed were not severely exposed.

There are a number of illnesses and occupations in which men have been reported to sire an excess of daughters and to display low testosterone and/or high gonadotropin levels. The illnesses include non-Hodgkin's lymphoma and multiple sclerosis. The occupational exposures include those men involved in driving, diving, and those exposed to the nematocide dibromochloropropane (DBCP). Table 1 provides the references that substantiate the excess of daughters and the above hormone profile. Other occupational exposures that are associated with low offspring sex ratios are related to high-voltage installations (6–8), sodium borates (9), and car-

bon setting (10). Such exposures may be suspected of disrupting men's hormone levels, but I know of no direct evidence to document this suspicion. Thus, low offspring sex ratio may be regarded as a useful noninvasive monitor of reproductive hazards to men. Little is known about the effects of such exposures on women.

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Response

In his letter, William H. James makes a valuable comment on our recent review on xenoestrogens (1) concerning reproductive effects of male exposure to dioxins. Whereas adverse reproductive effects of dioxin in laboratory animals are well documented (2), data on exposed human populations are scarce. The novel studies on offspring sex ratios of dioxin-exposed people are therefore very intriguing. Exposure to dioxins is associated with low male-female offspring ratio (3,4). Although this type of skewed sex ratio has been hypothesized to reflect impaired fertility, the underlying mechanisms have remained elusive. James (5) has suggested that parental hormone levels at the time of conception partially control mammalian sex ratio at birth. However, there is not enough experimental evidence to prove the hypothesis, and again, we do not have a theoretical basis for understanding the determination of sex ratio. Thus, both reproductive effects of dioxins and determination of sex ratio are research areas that need more of our attention.

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Table 1. Male illnesses and occupational exposures associated with low offspring sex ratio and high gonadotropin and/or low testosterone levels.

Illnesses	References	
	Low offspring sex ratio	Hormone profile
Non-Hodgkin's lymphoma	(11)	(12)
Multiple Sclerosis	(13)	(13)
Exposures		
Professional Driving	(14)	(15)
Professional Diving	(16,17)	(18)
Use of DBCP	(19)	(20)